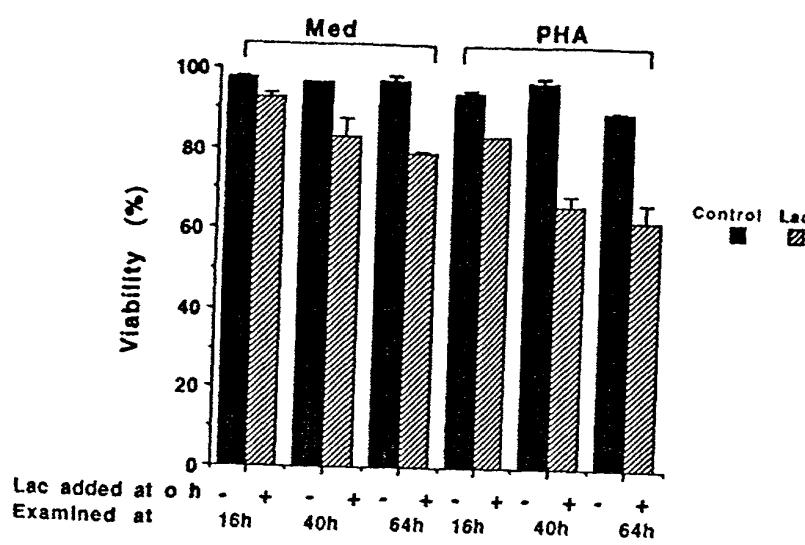
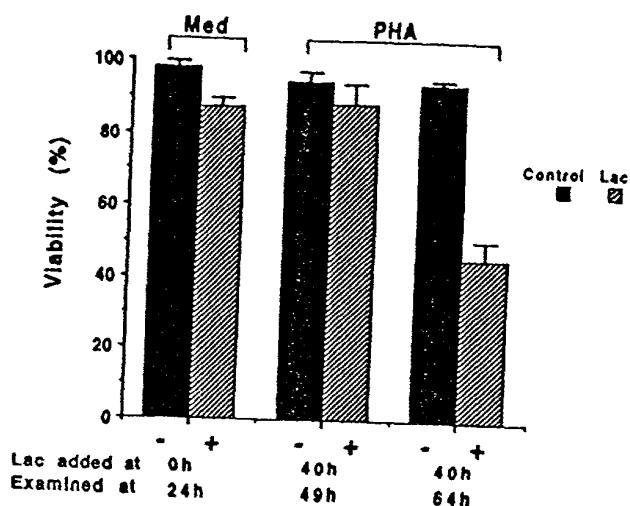


FIGURE 1

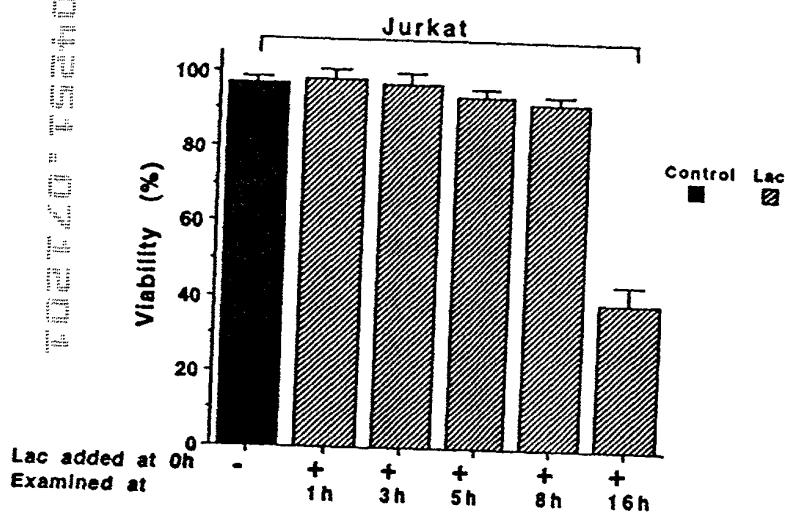
a



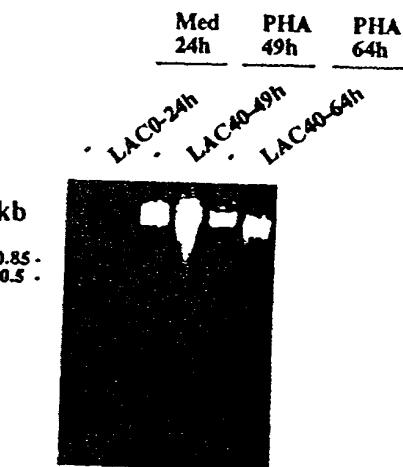
b



c



d



e

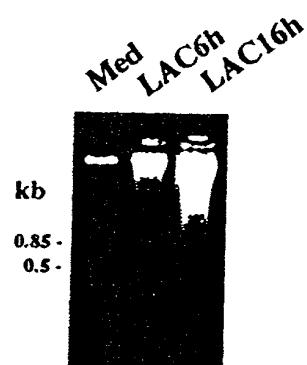


FIGURE 2

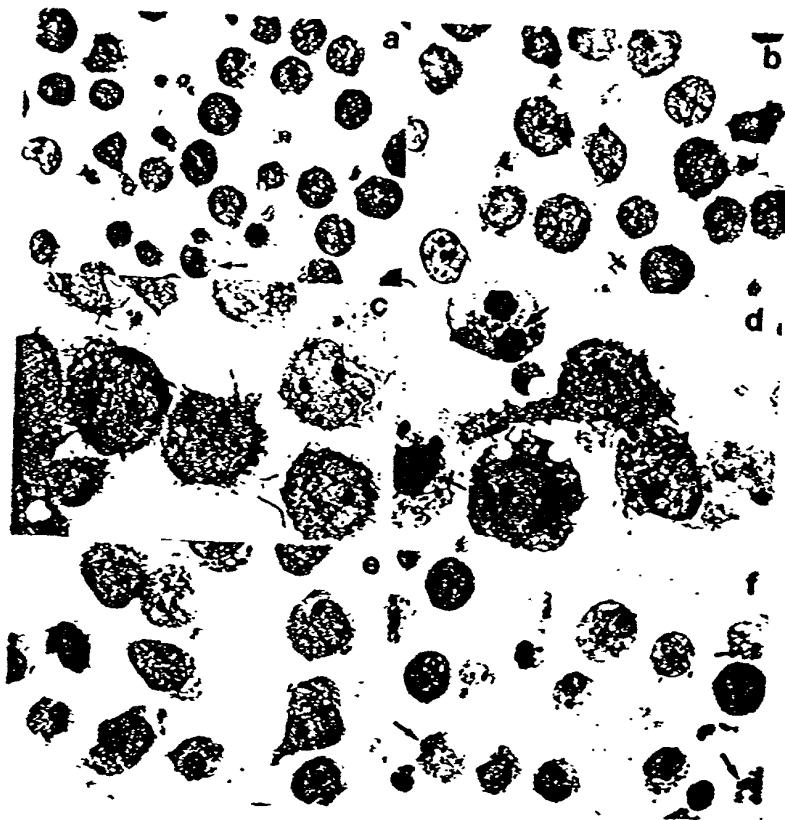
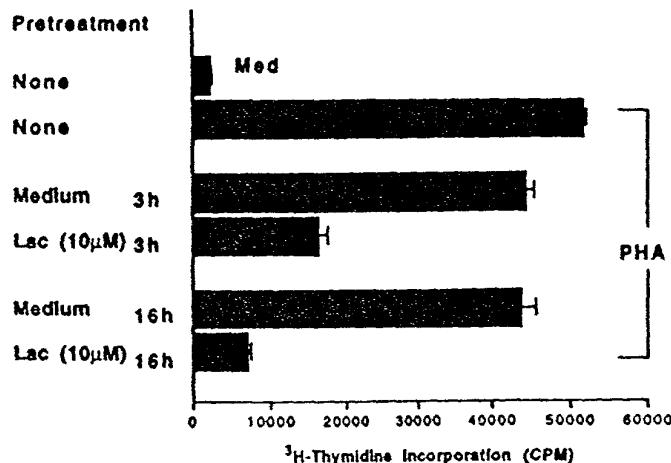
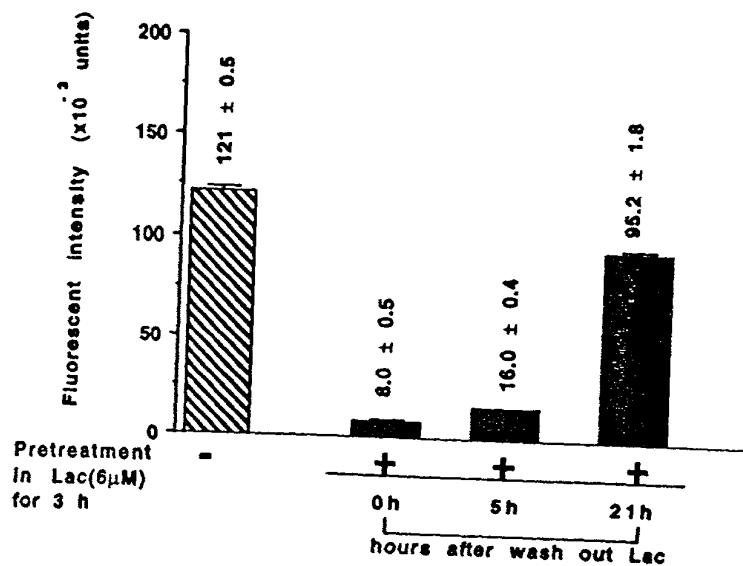


FIGURE 3

A



B



C

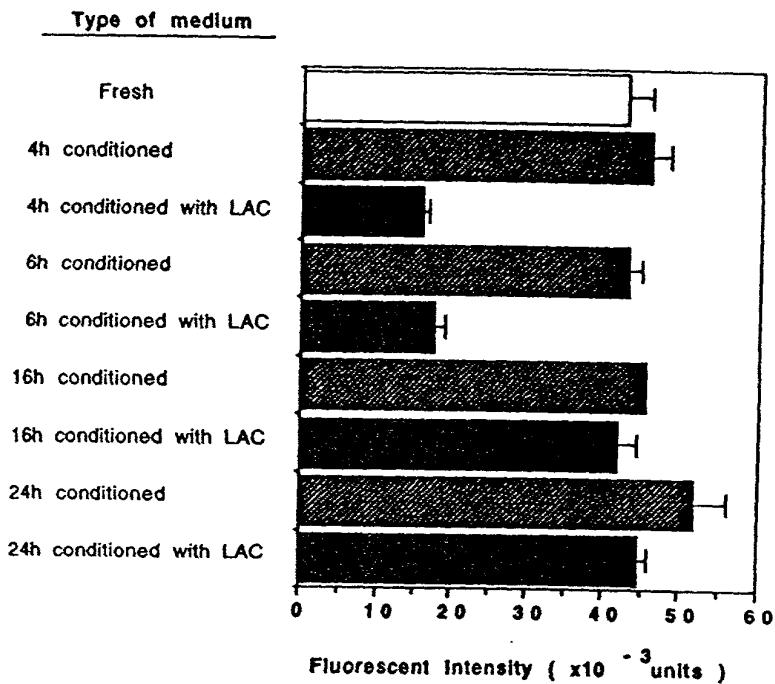


FIGURE 4

a **Medium** **LAC**

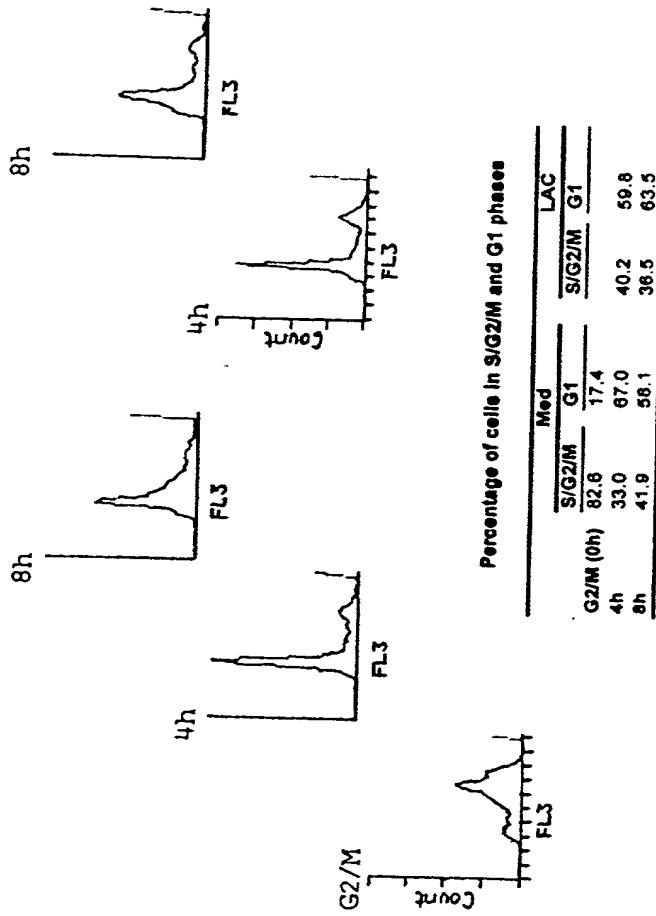


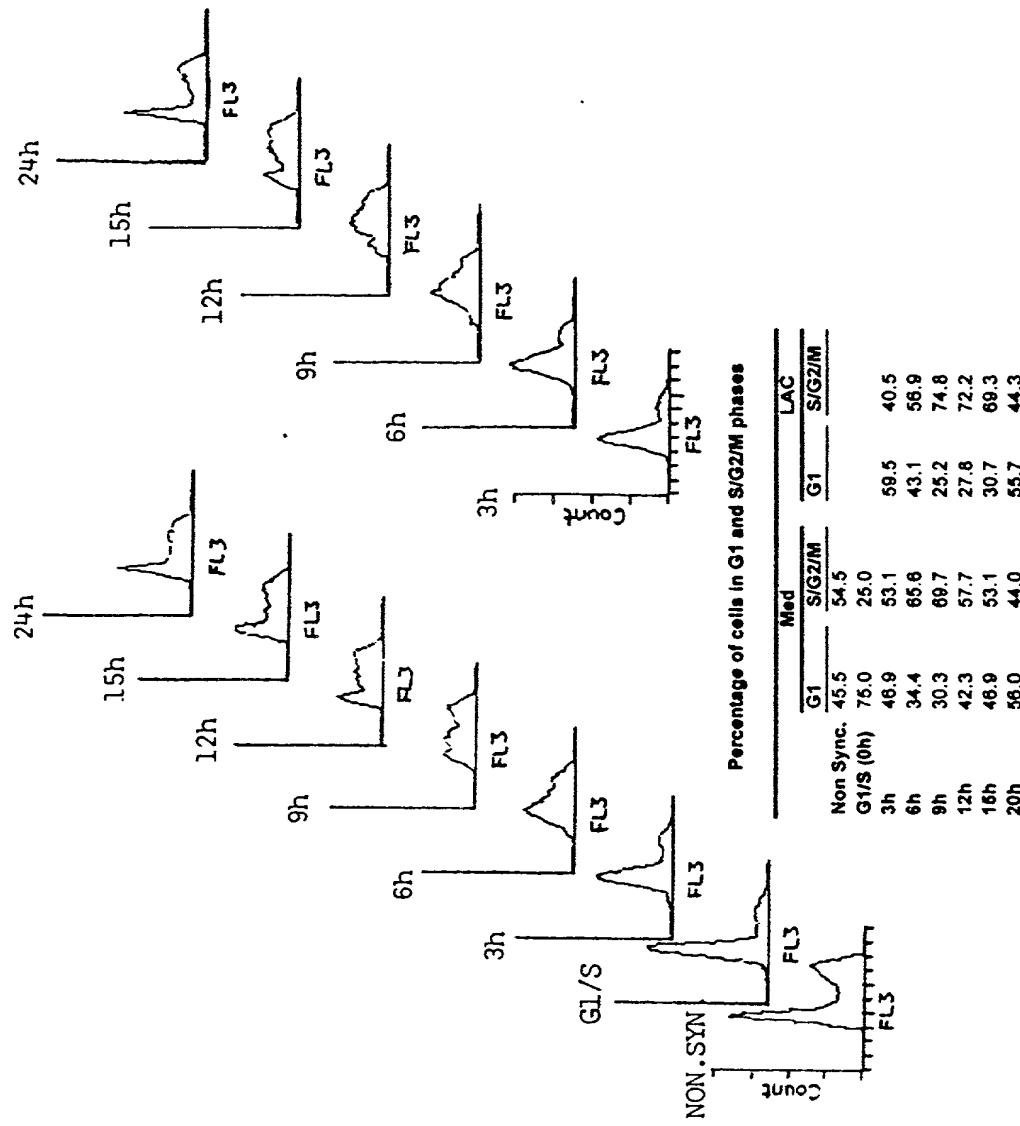
FIGURE 6A

卷之三

2

Medium

LAC



Attender: WU
Docket No.: 95594US1
Title: USE OF PROTEASOME INHIBITORS FOR TREATING CANCER.
Inventor: MURTHY, VENKATESWARA
Assignee: GENENTECH, INC.
Attorney Name: Serebriakoff, George
Phone No.: 612-336-4728
Fax No.: 612-336-4728
Priority Date: 07/03/1997
Filing Date: 07/03/1997
Issue Date: 07/03/1997
Status: Active
Classification: 435/285.1
Abstract: The present invention relates to the use of proteasome inhibitors for the treatment of cancer. The invention also relates to the use of proteasome inhibitors for the treatment of other diseases, such as autoimmune diseases, graft rejection and septic shock.

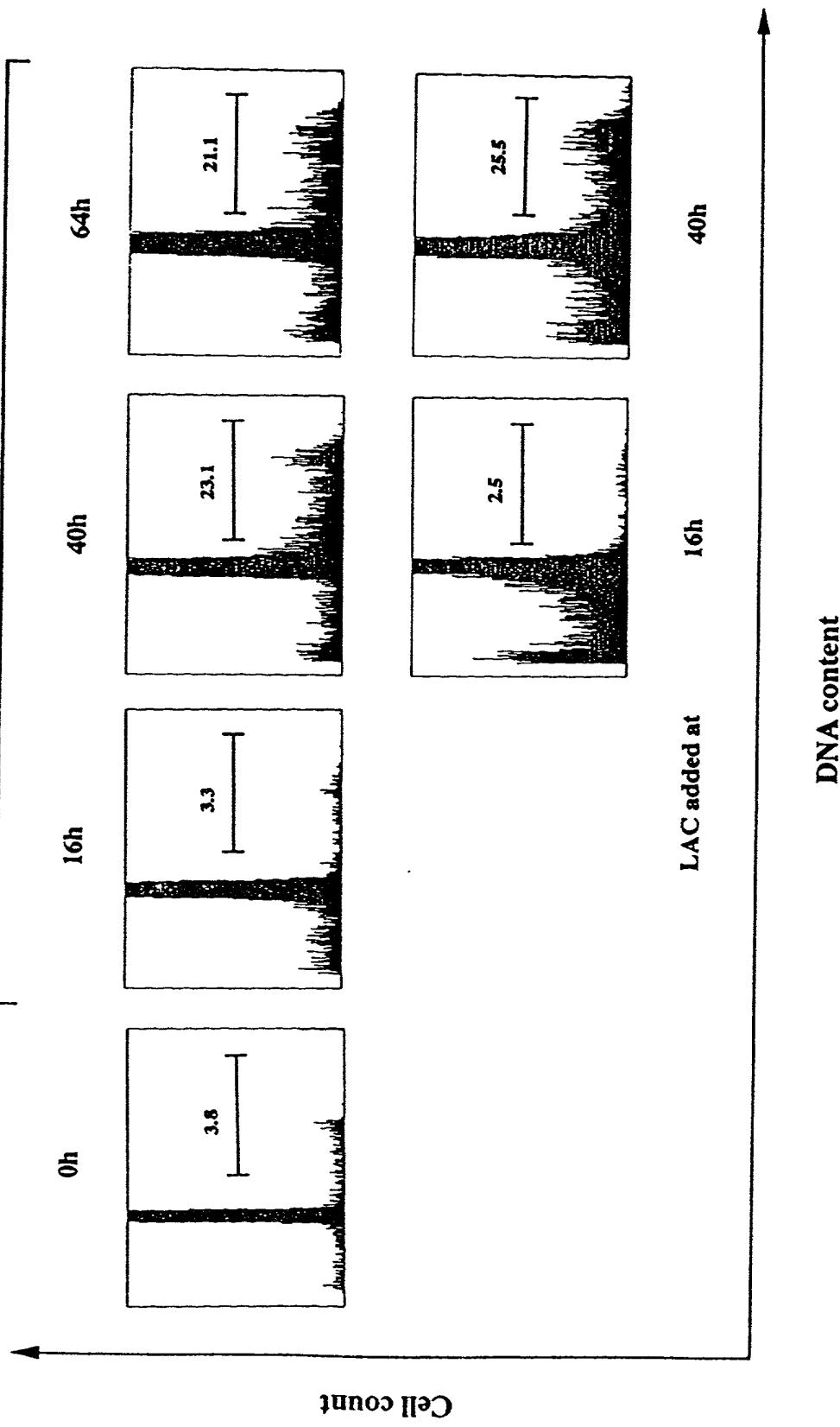
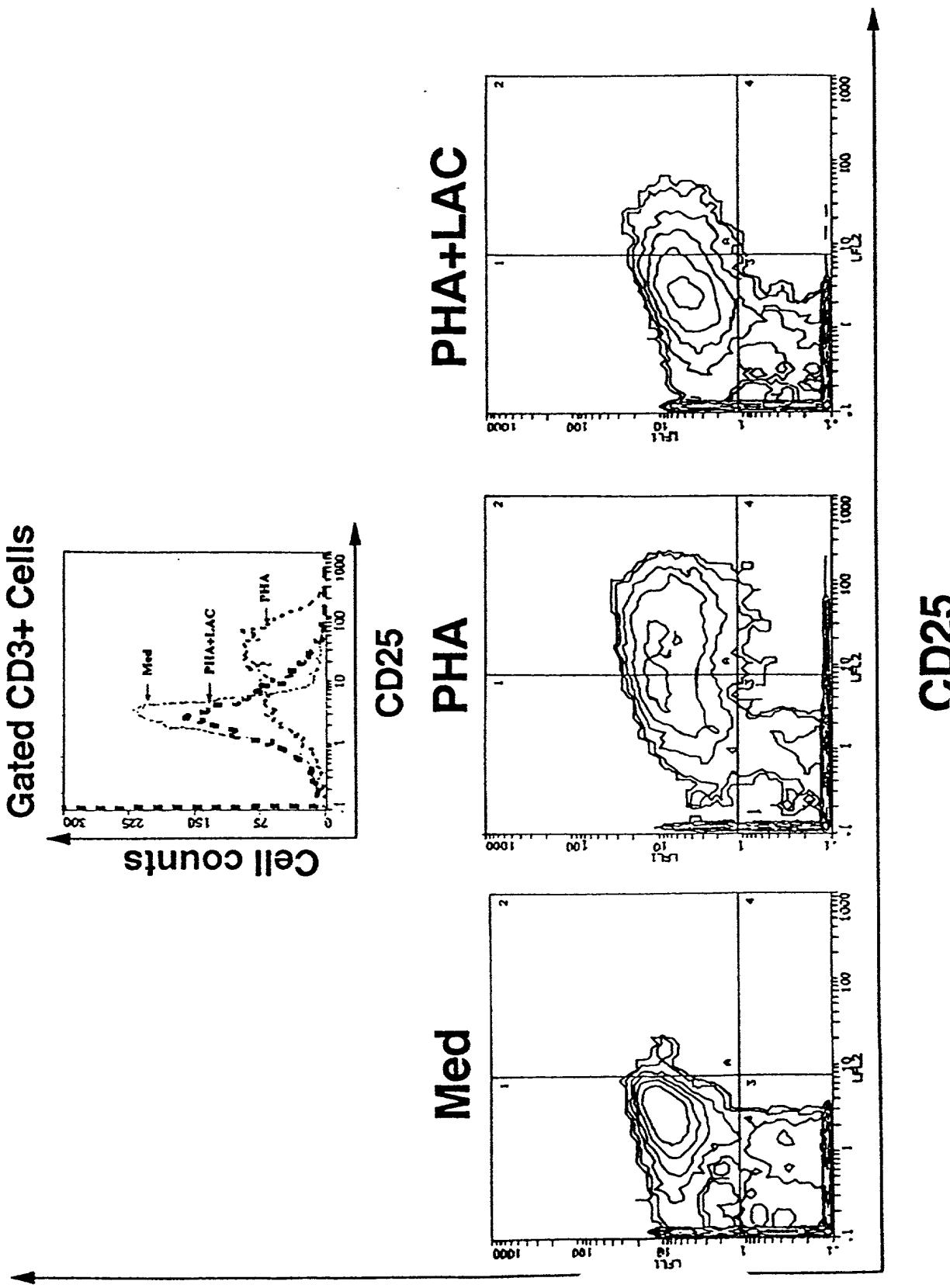
C**PHA**

FIGURE 6C

FIGURE 5



d

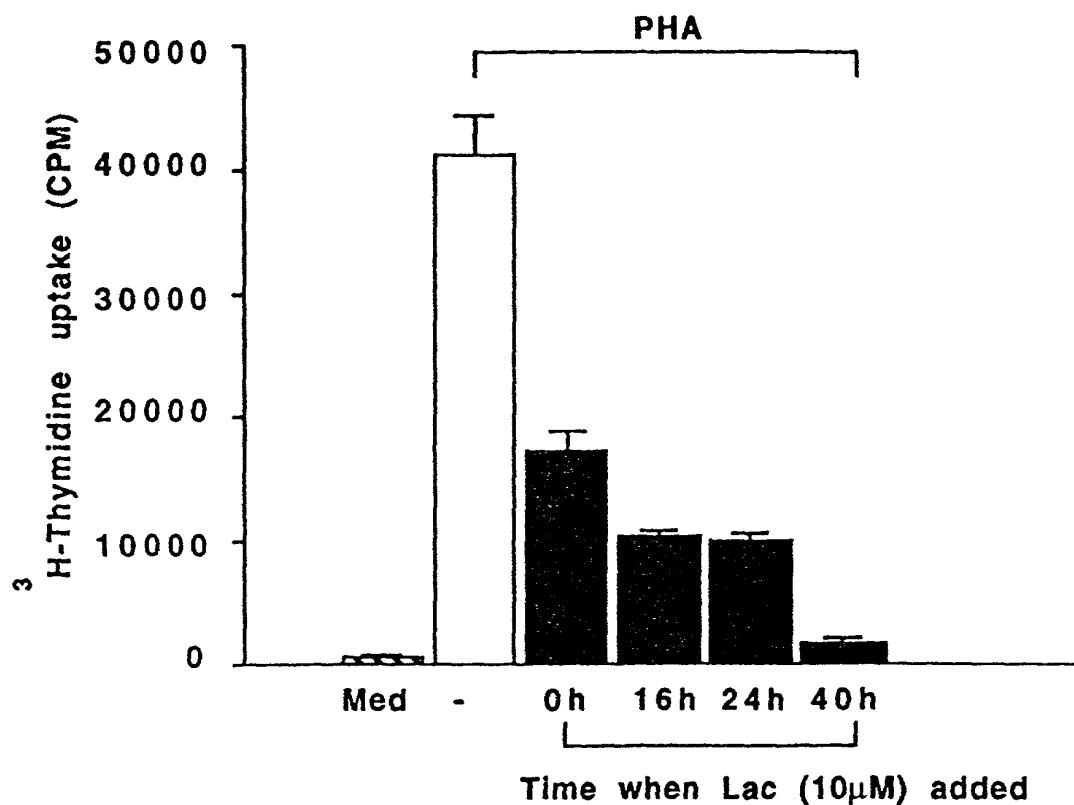


FIGURE 6D

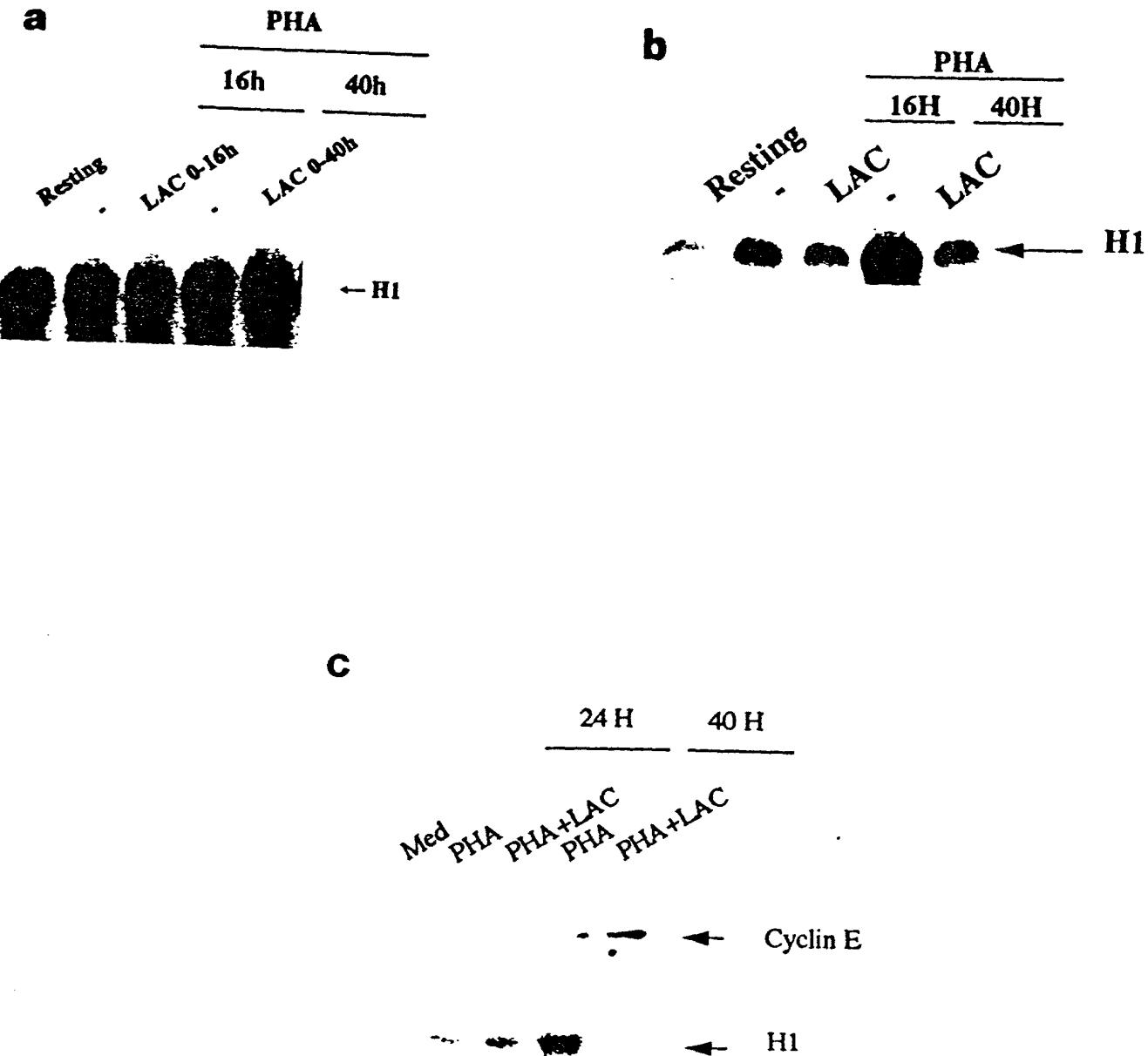
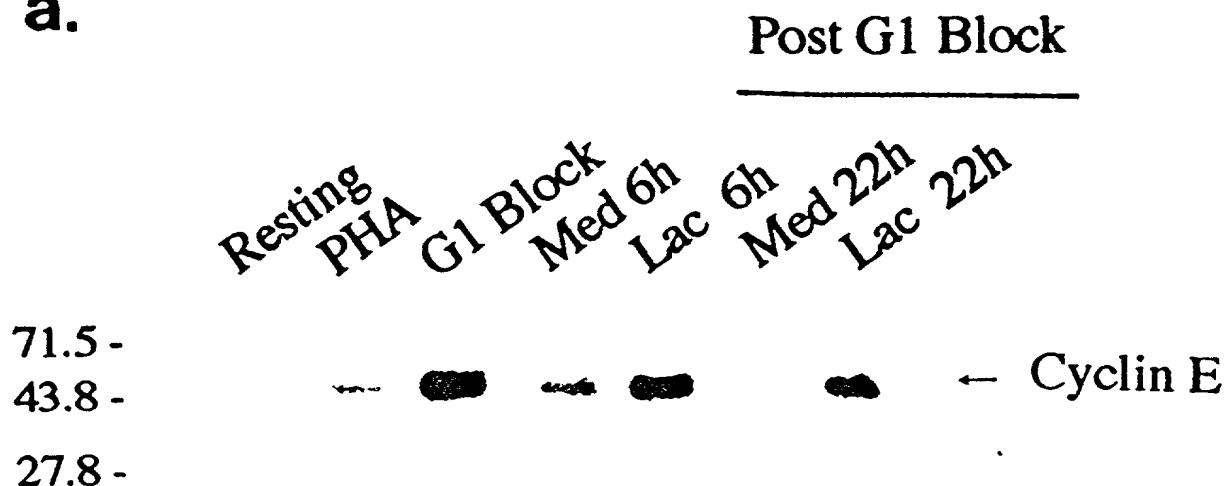


FIGURE 7

a.



b.

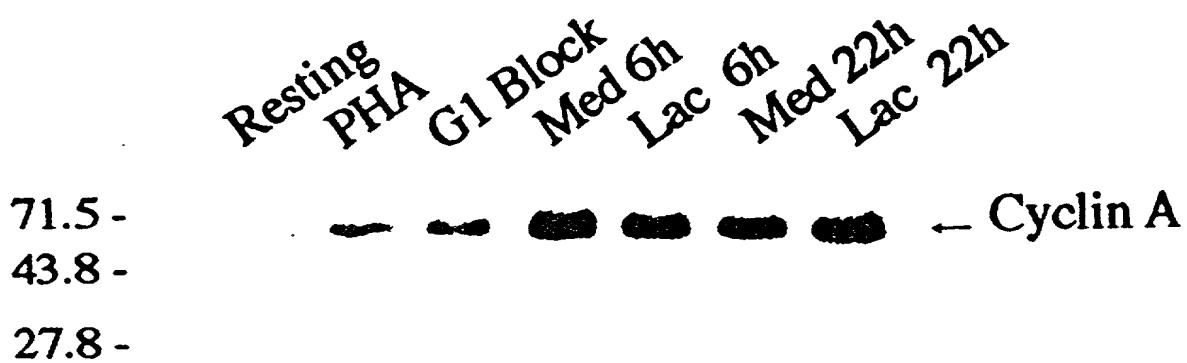
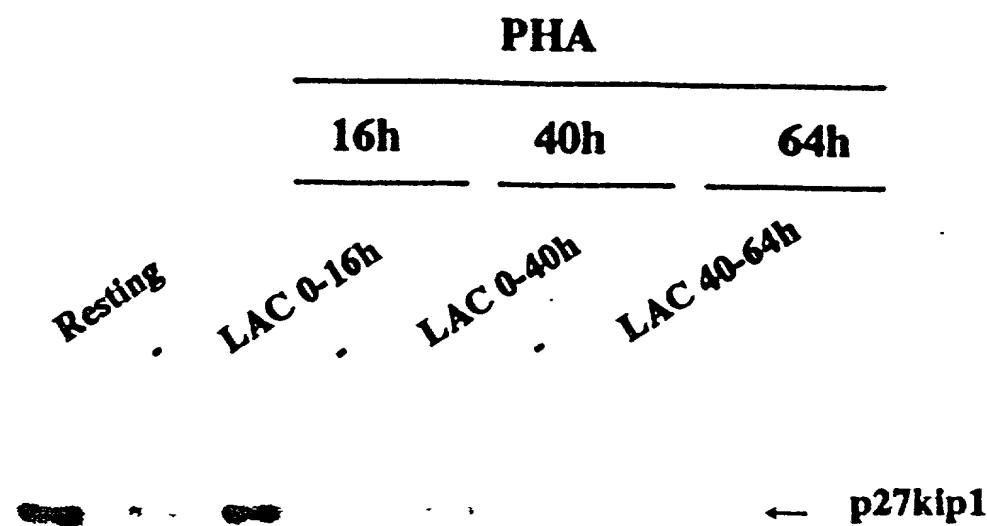


FIGURE 8

a.



b.

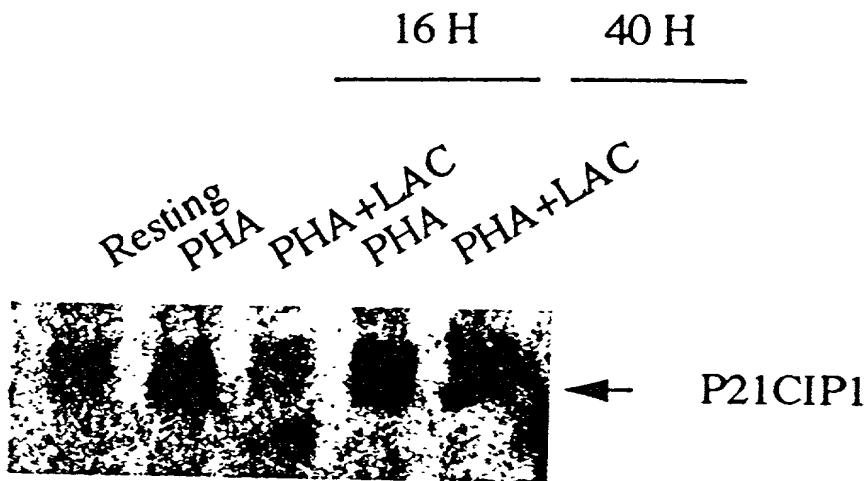


FIGURE 9

**Lactacystin inhibits aggregation of
PHA-stimulated human PBMC**

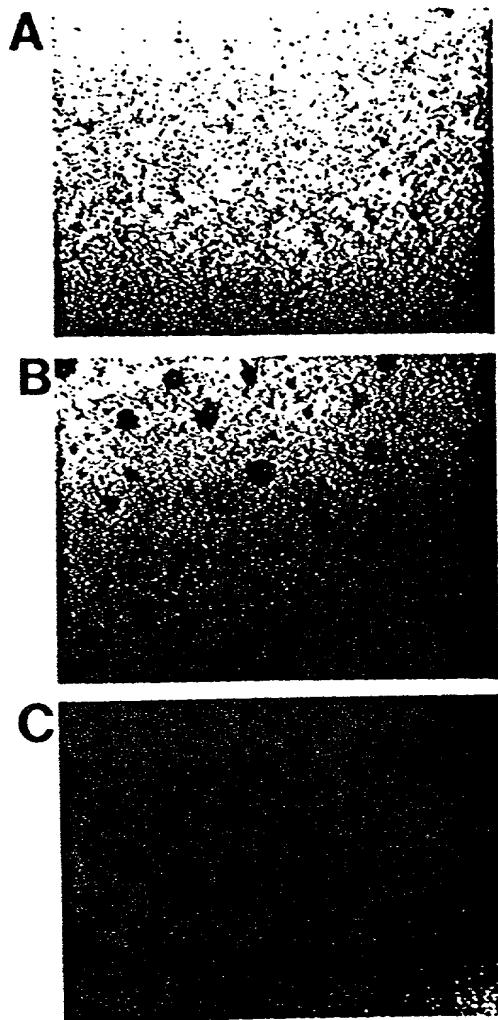


FIGURE 10

**Lactacystin inhibits aggregation of
mitogen-stimulated mouse lymph node cells**

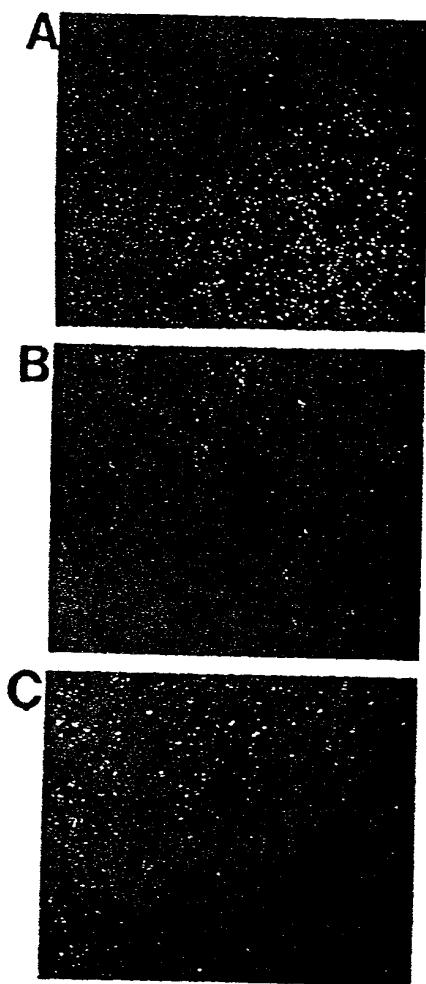
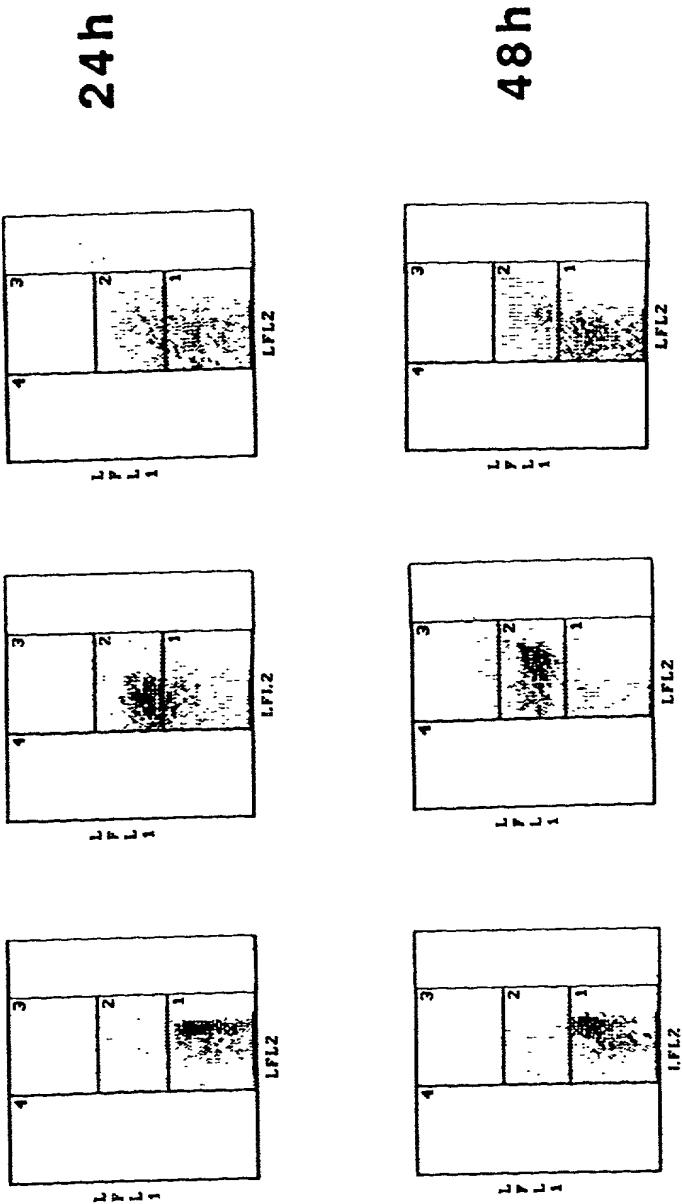


FIGURE 11

Med Con A Con A+Lac



ICAM-1 (LFL1)

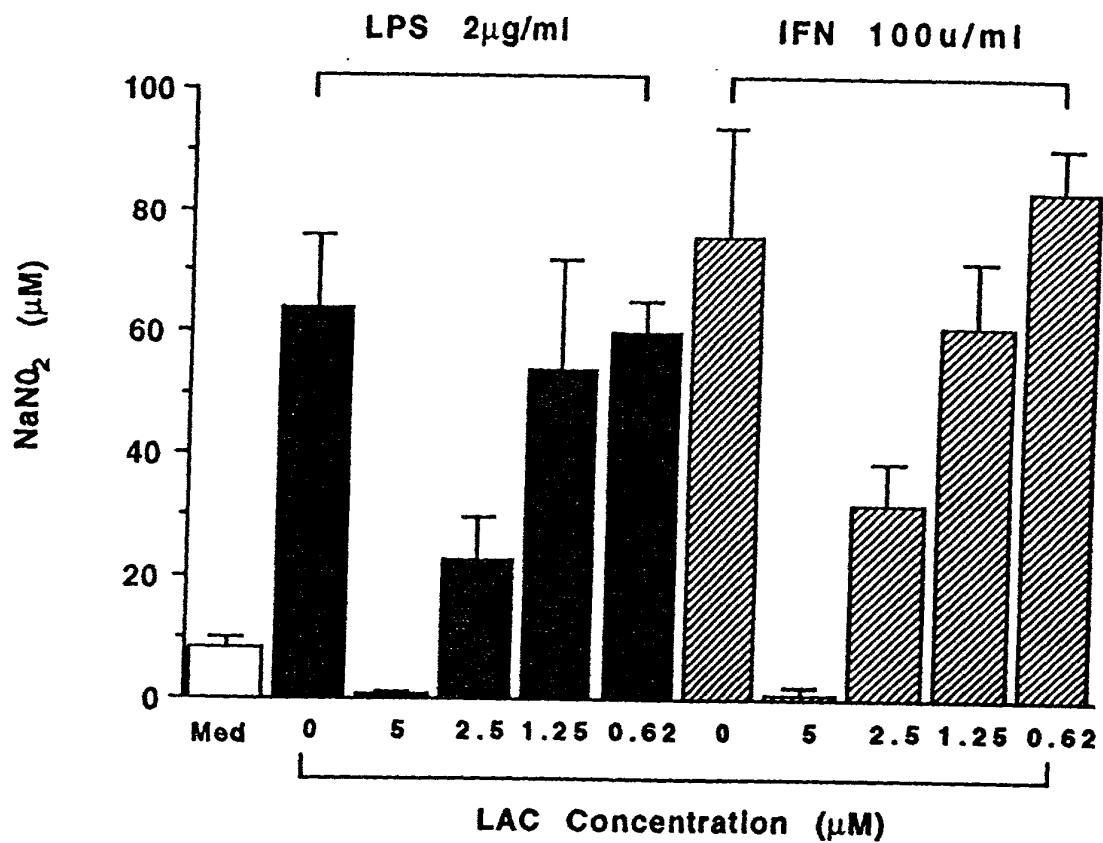


FIGURE 13

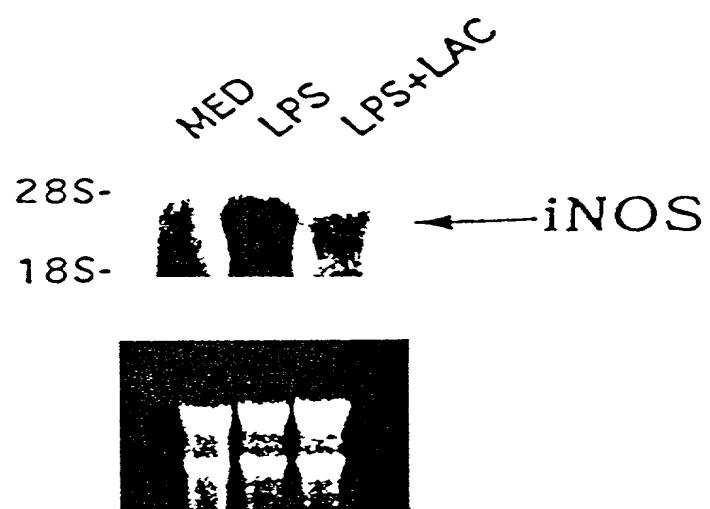


FIGURE 14

FIGURE 15

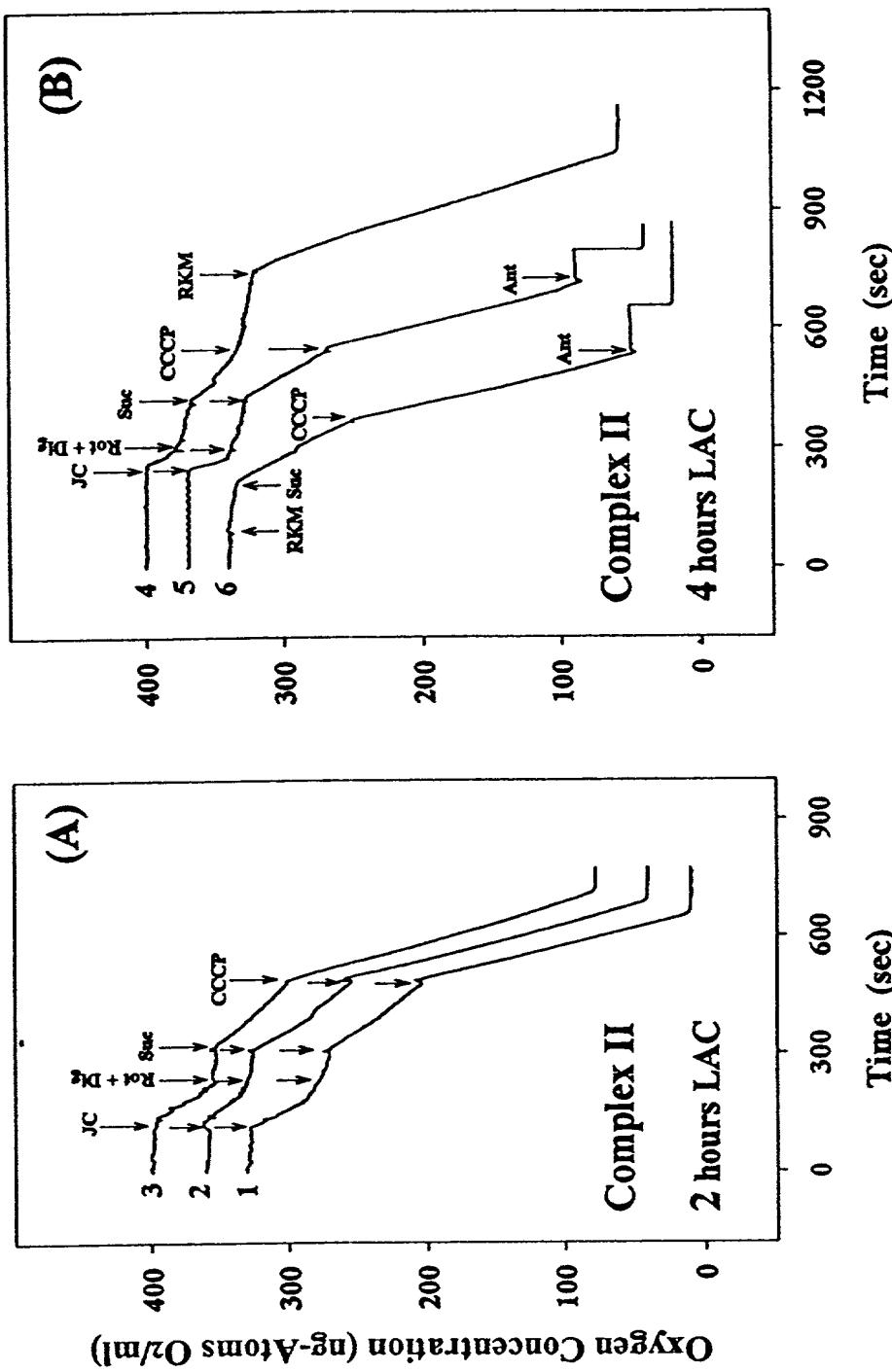


FIGURE 16

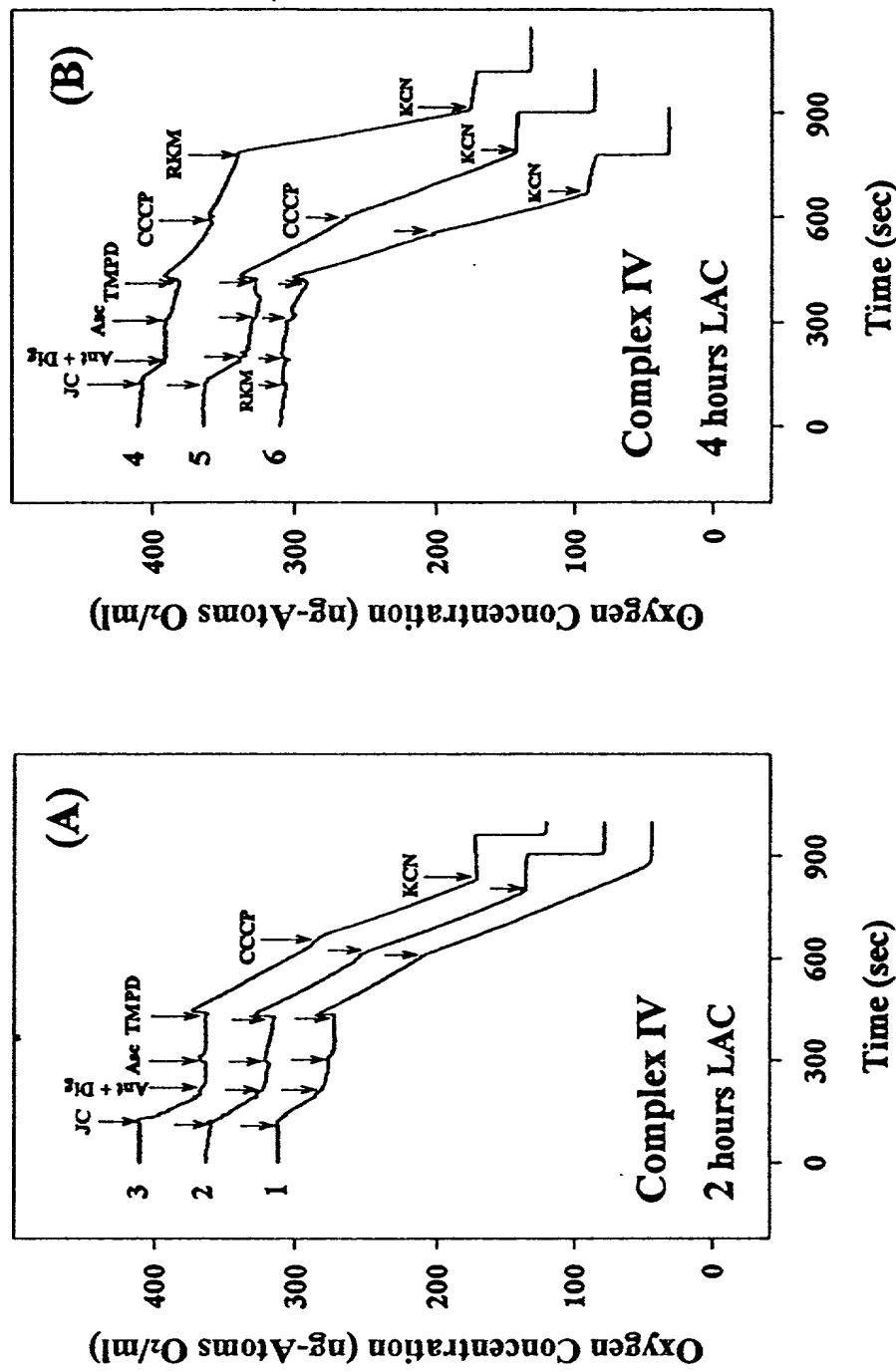
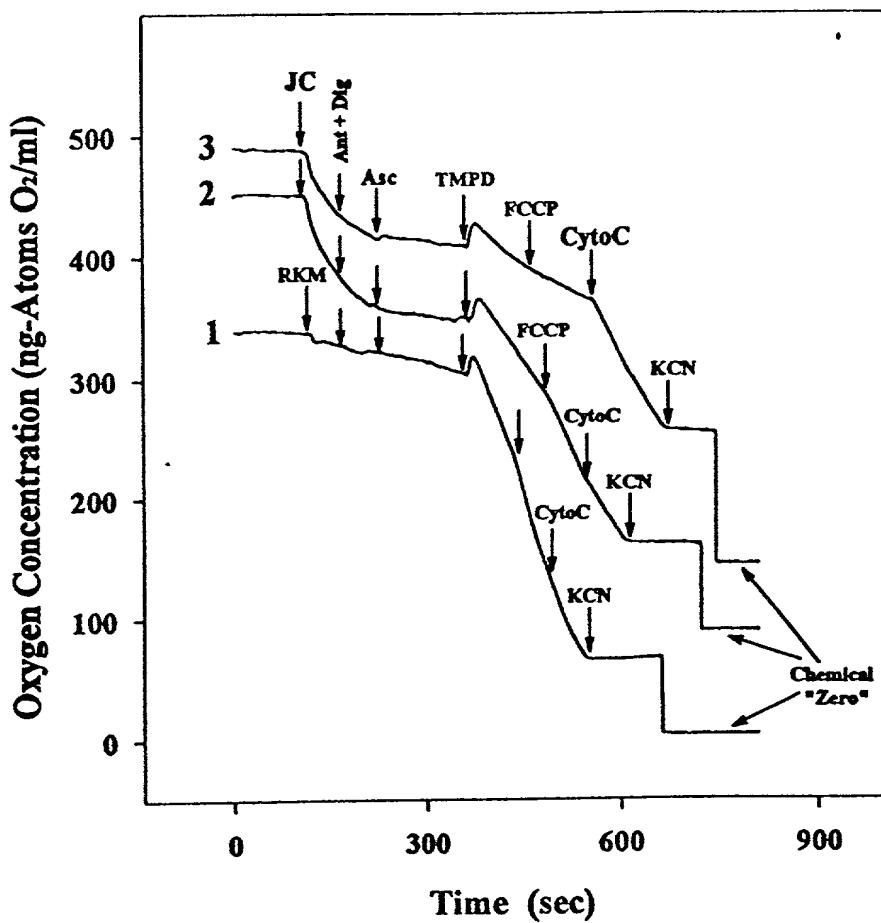


FIGURE 17



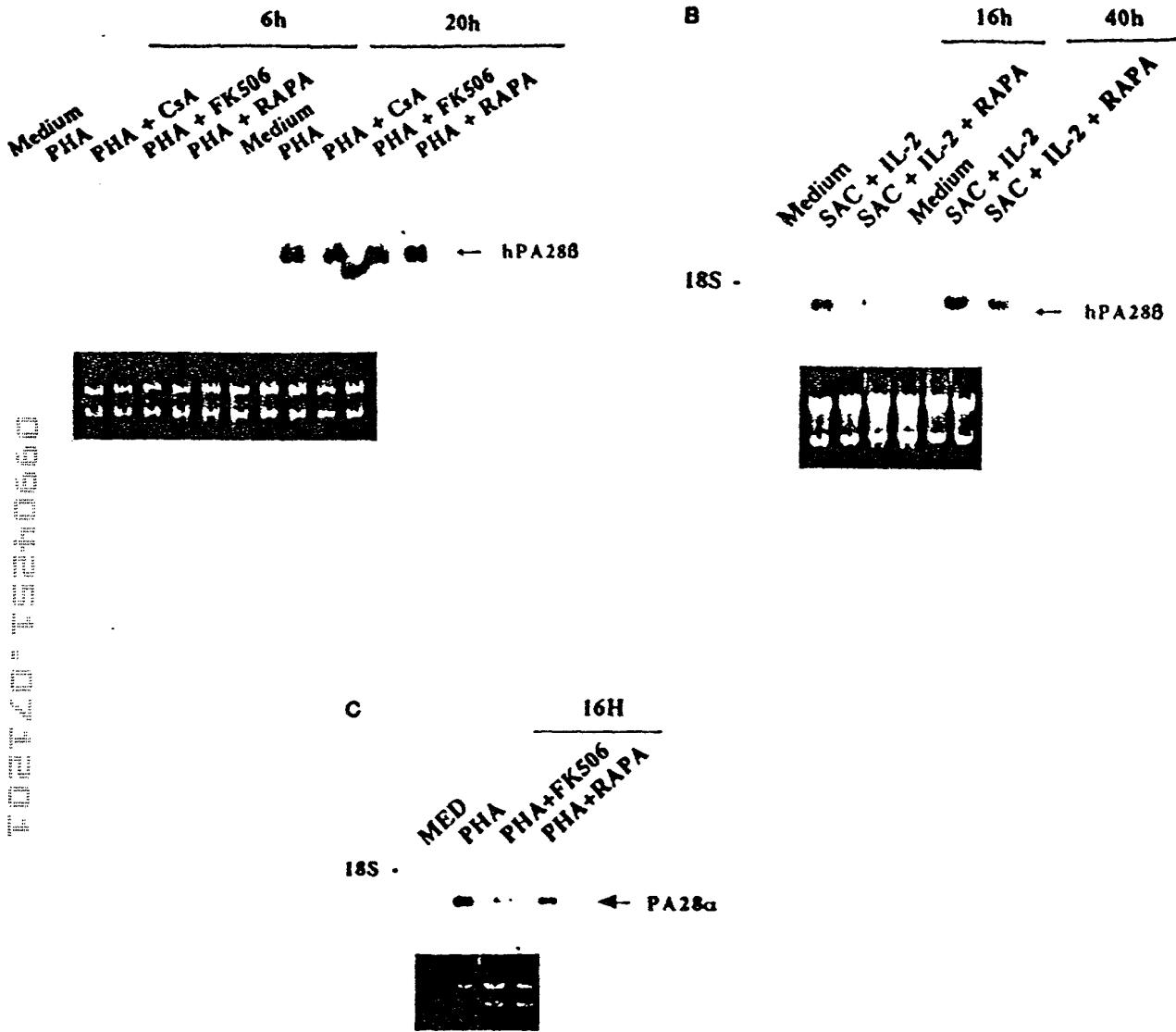


FIGURE 18

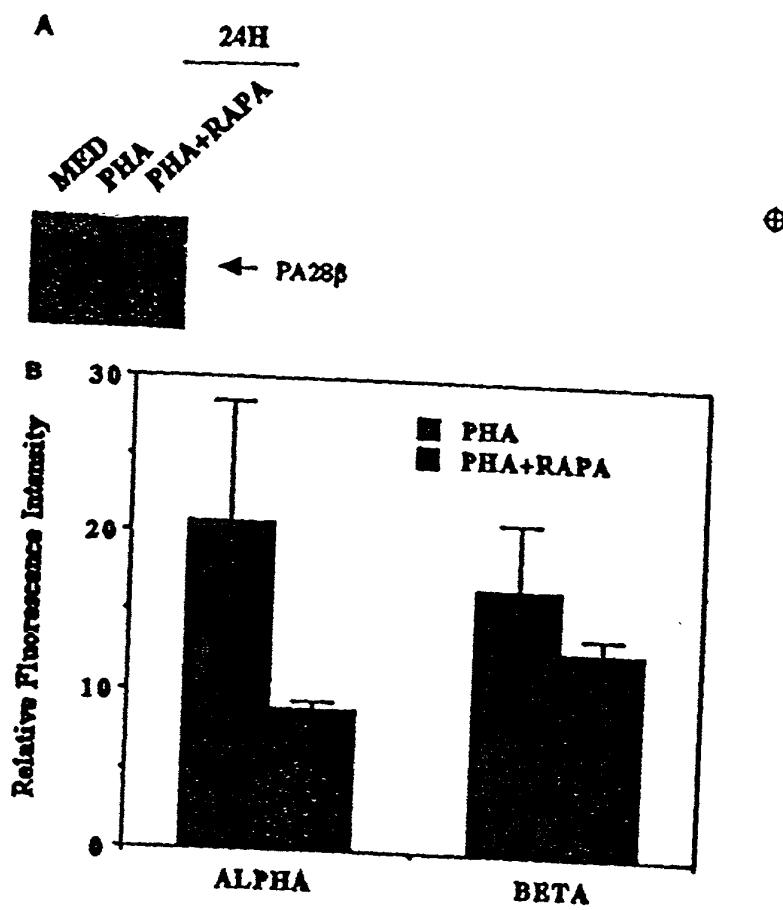


FIGURE 19

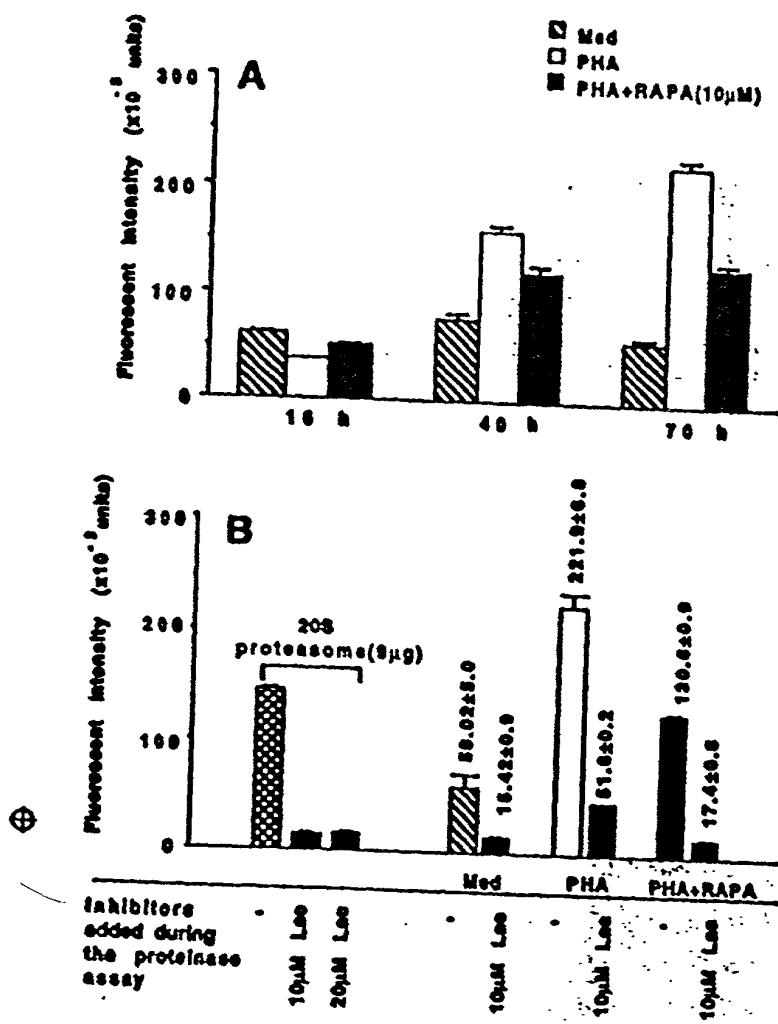


FIGURE 20

Eliminating Alloantigen-specific Response by a Proteasome Inhibitor

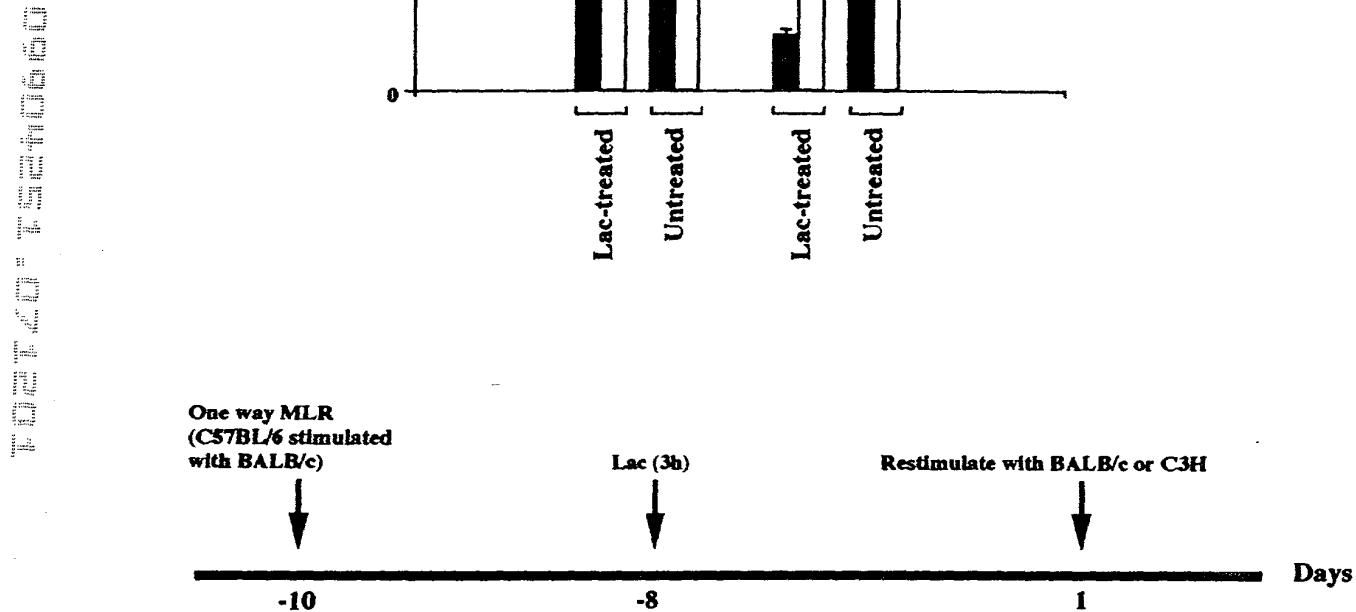
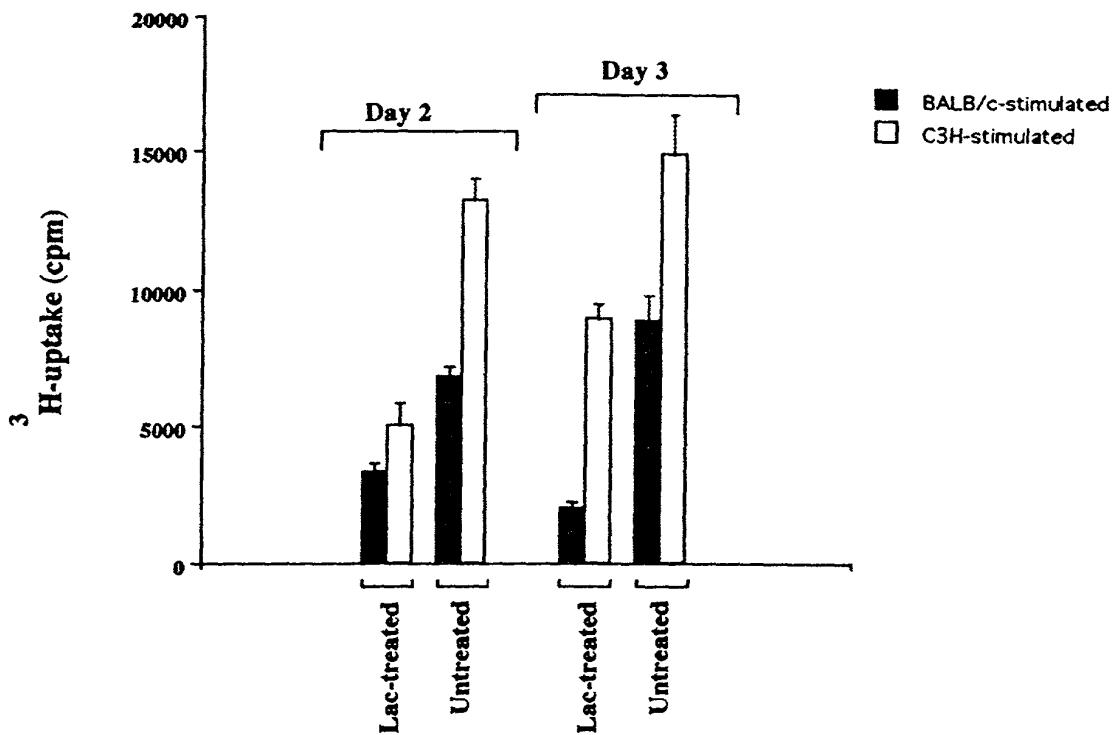


Fig. 21

Z-VAD.fmk blocks Lactacystin induced apoptosis in Jurkat cell

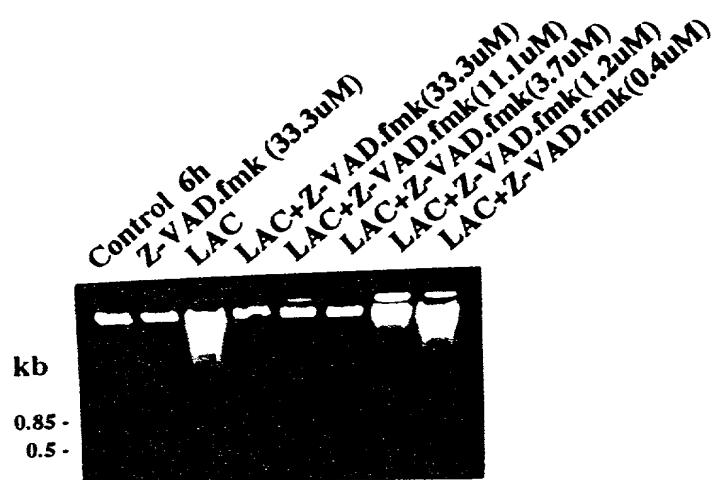
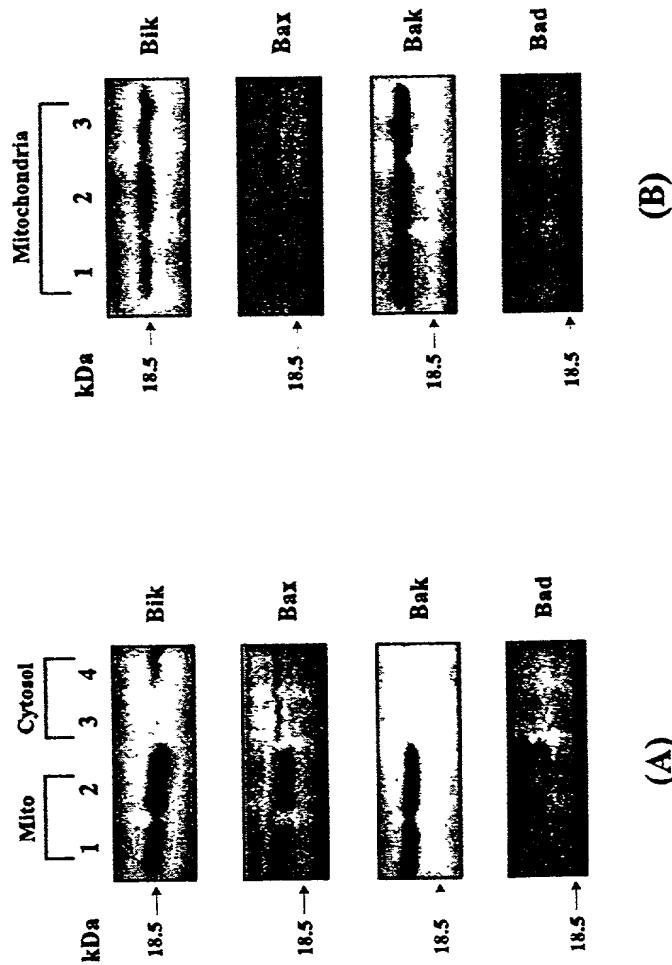


Fig. 22

Fig. 23



DNA-fragmentation in Namalwa-Control (■) and Namalwa-BclX_L (▨) cells during Lactacystin (LAC) induced apoptosis.

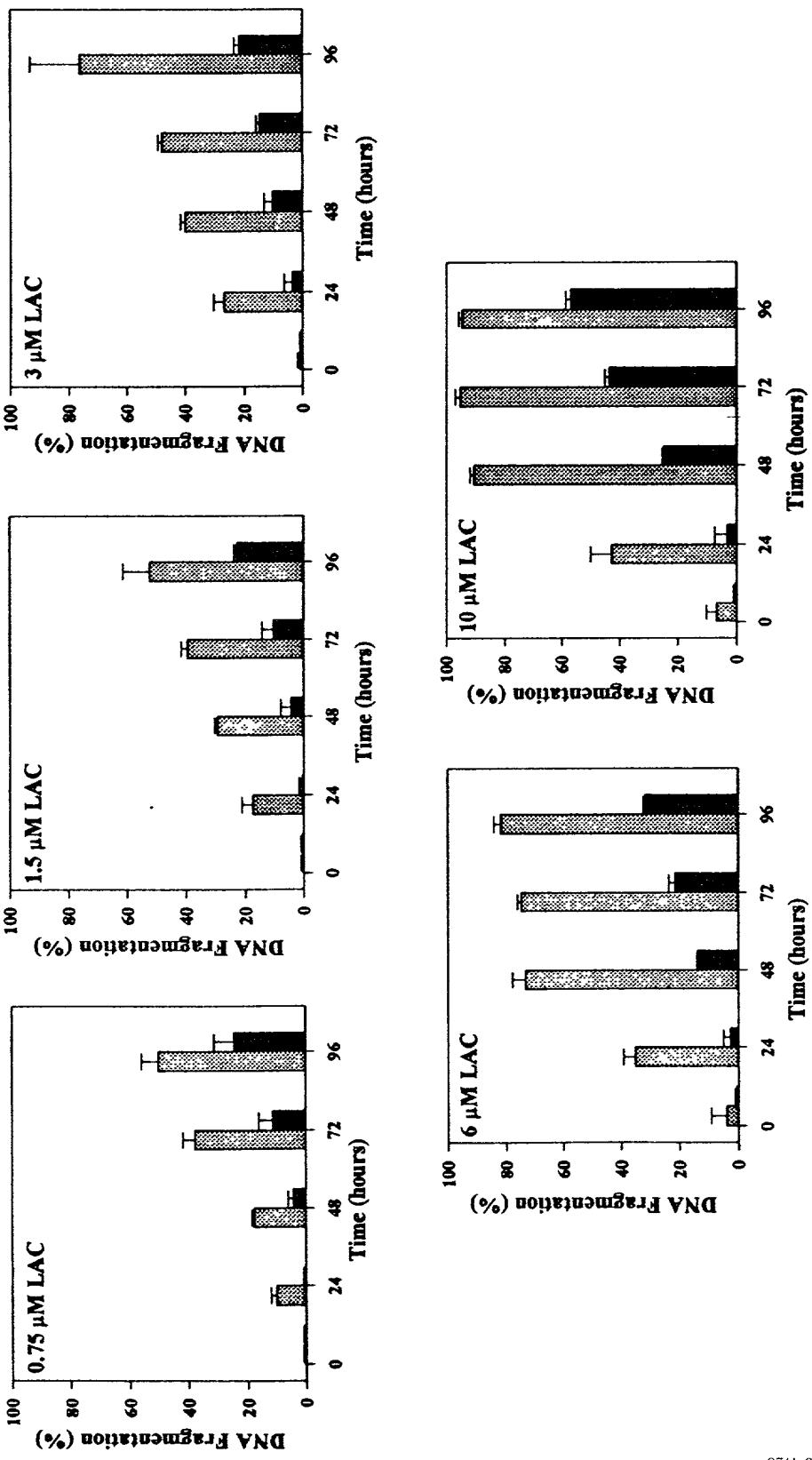
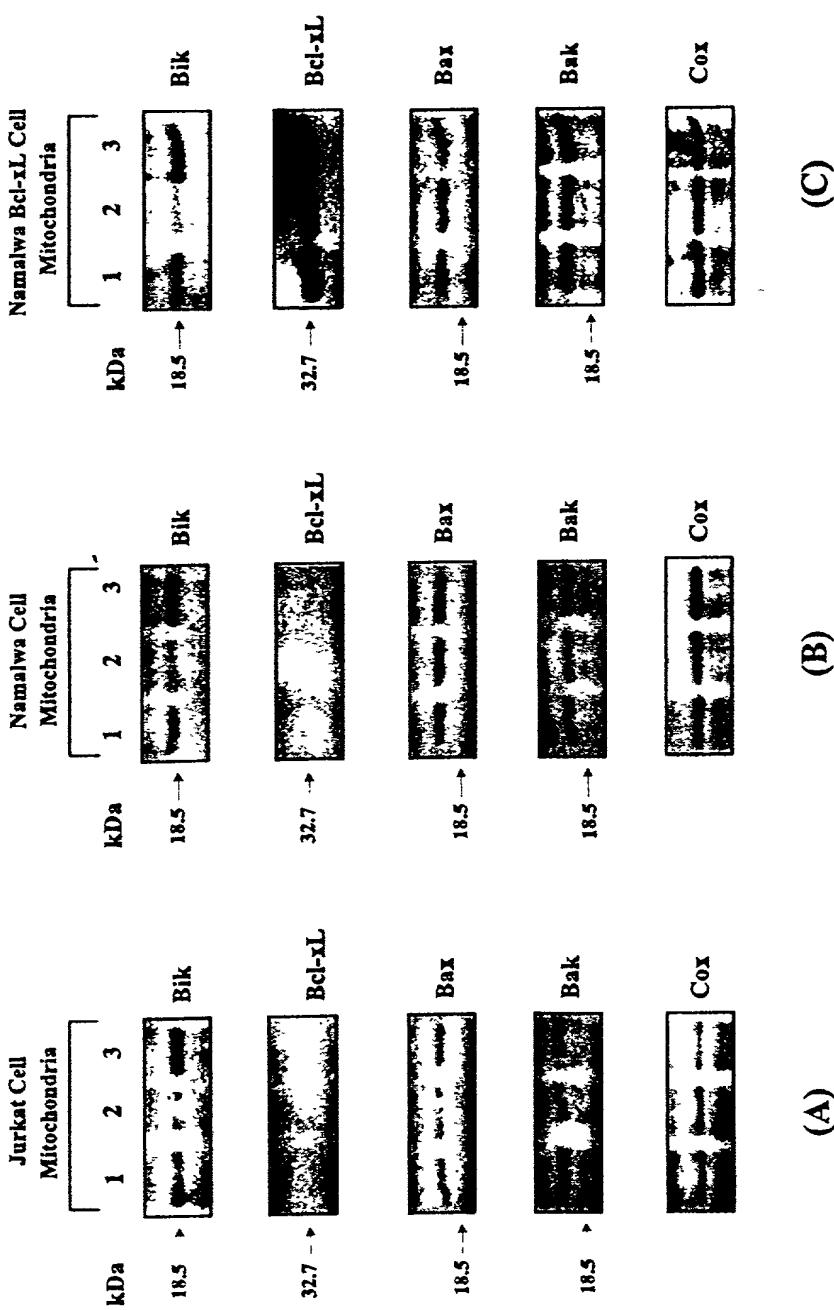


Fig. 24

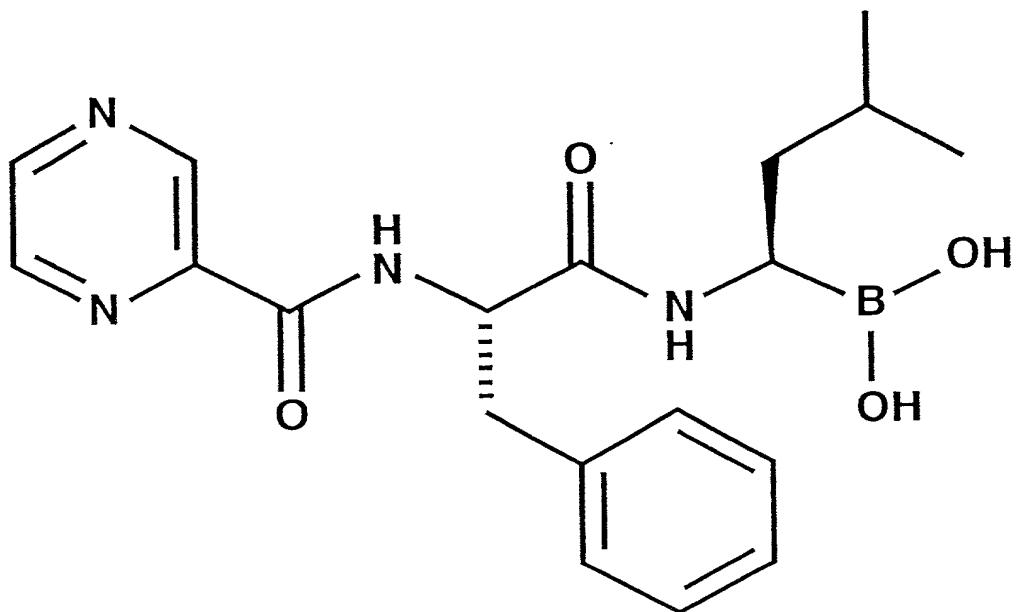
Fig. 25



Sheet 28 of 34
 Title: USE OF PROTEASOME INHIBITORS FOR TREATING CANCER
 INFLAMMATION, AUTOIMMUNE DISEASE, GRAFT REJECTION AND SEPTIC SHOCK
 Attorney Name: Gregory A. Sebold
 Phone No.: 612-336-4728
 DocID: 955540US1
 Inventor: WU
 Interim: USE OF PROTEASOME INHIBITORS FOR TREATING CANCER
 Attorney Name: Gregory A. Sebold
 Phone No.: 612-336-4728
 DocID: 955540US1

DIPEPTIDE BORONIC ACID (DPBA)

Pyz-Phe-boroLeu; Pyz, 2,5-pyrazinecarboxylic acid



LACTACYSTIN

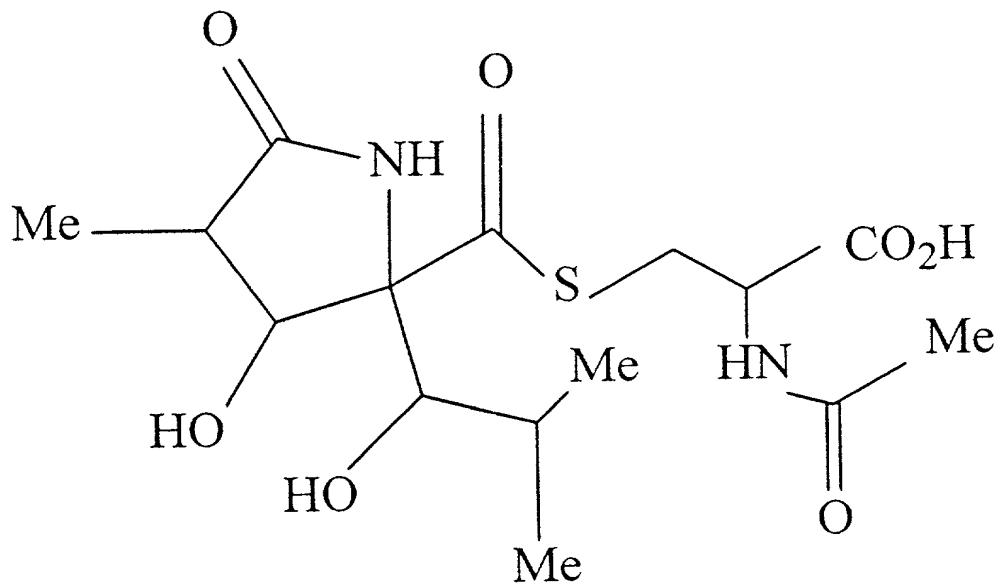


FIGURE 26

DPBA INHIBITS 20S PROTEASOME ACTIVITY

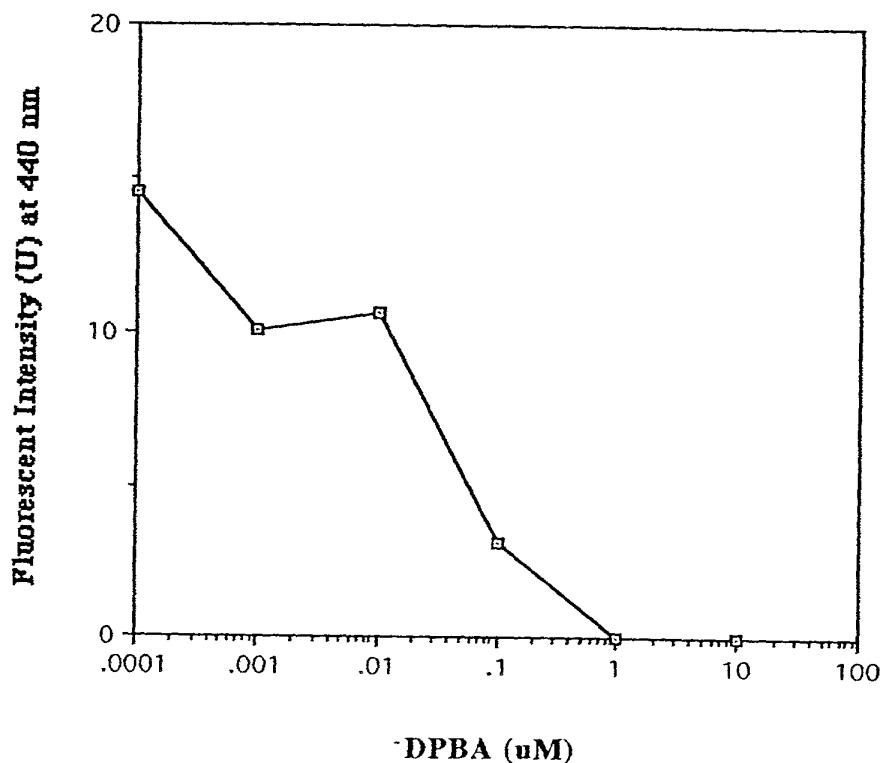


FIGURE 27

Proteasome Inhibitor DPBA Inhibits Anti-CD3 Stimulated T Cell Proliferation

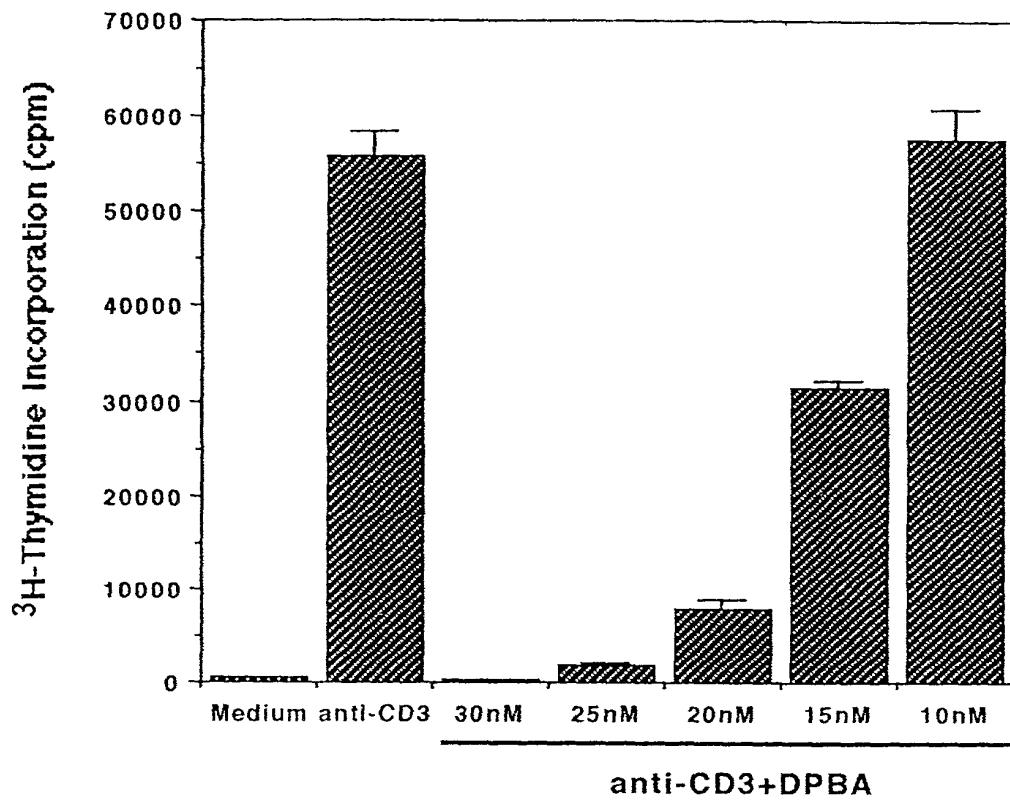
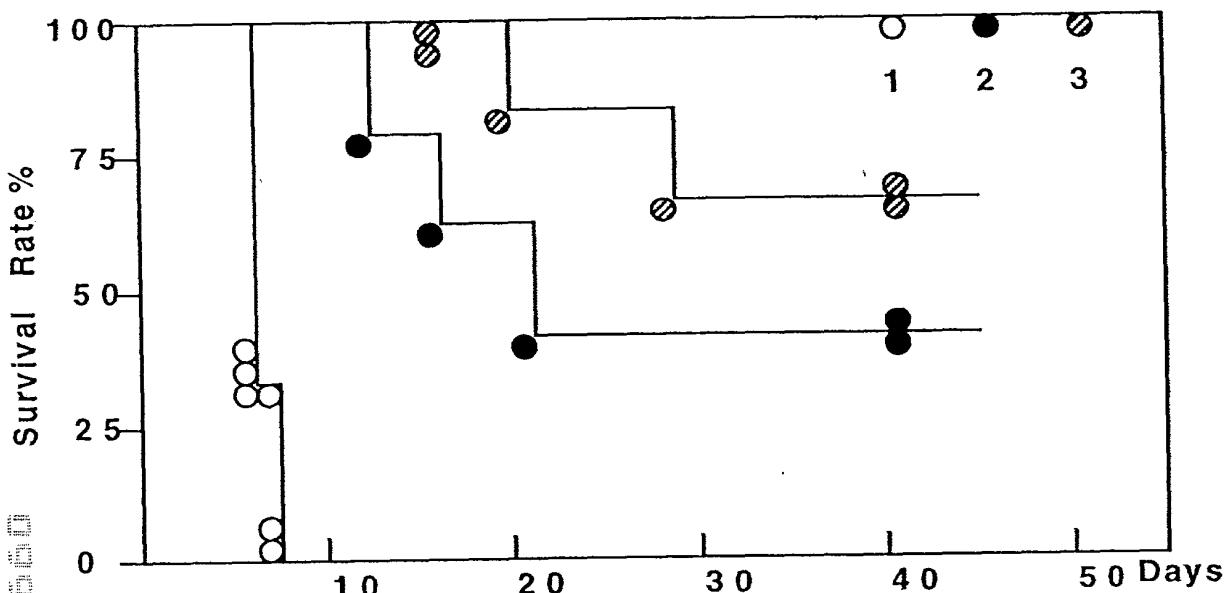


FIGURE 28

Proteasome Inhibitor DPBA Prolongs Mouse Heart Allograft Survival



Groups	Survival Days	MST \pm SD	p value
1 Control	7, 7, 7, 7, 8, 8	7.3 \pm 0.5	—
2 DPBA 0.65mg/kg x 16 days	13, 16, 21 >40, >40, >16	>26.1 \pm 13	0.006
3 DPBA 1.0mg/kg x 4 days, then 0.5mg/kg x 12 days	20, 29,>40 >16, >16 >16	>22.8 \pm 9.8	0.008

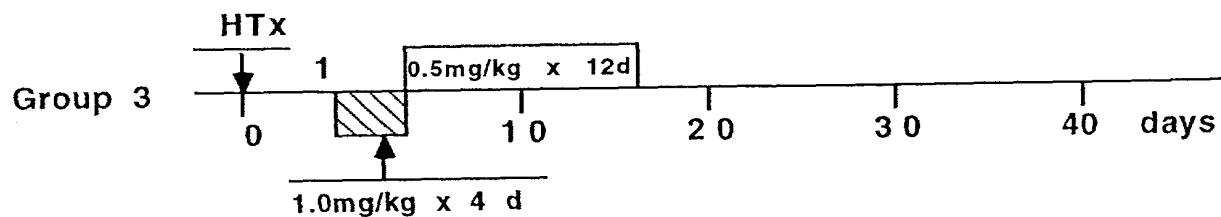
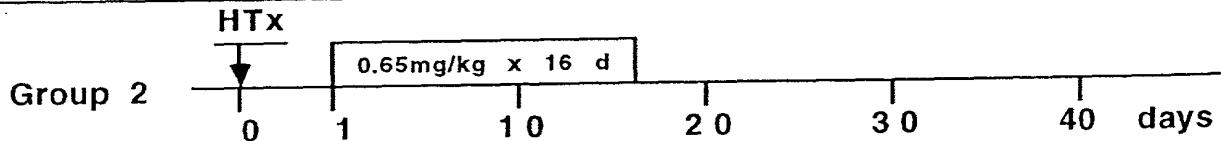
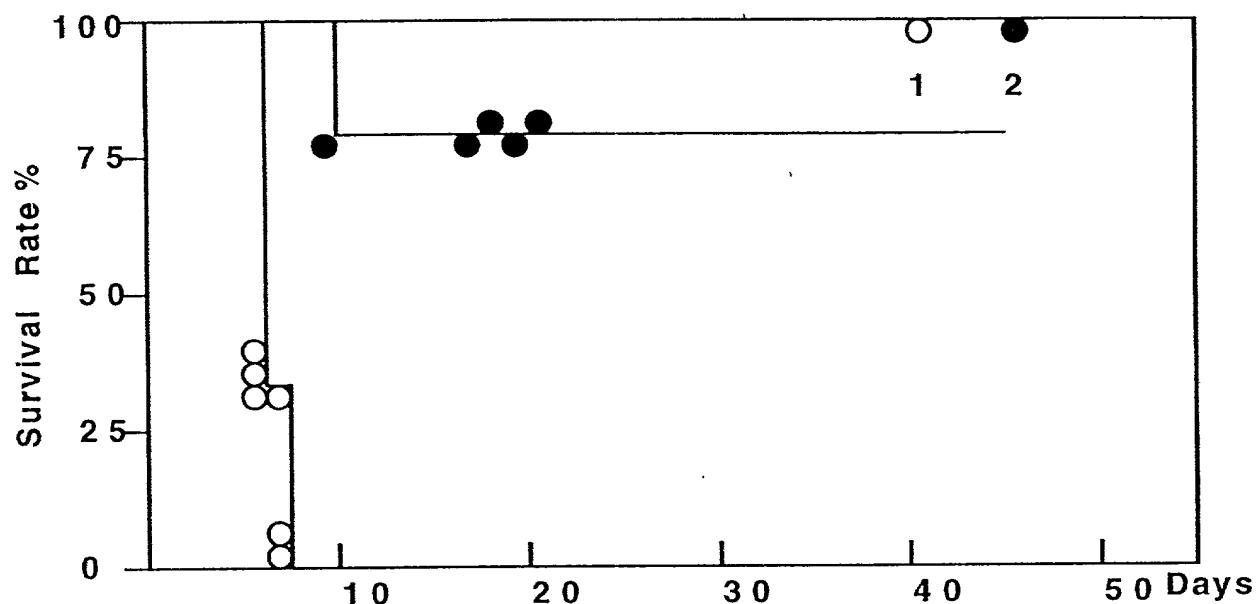


FIGURE 29

Proteasome Inhibitor DPBA is Effective in Treating Ongoing Heart Allograft Rejection in Mice



Groups	Survival Days	MST \pm SD	p value
1 Control	7, 7, 7, 7, 8, 8	7,3 \pm 0.5	-
2 DPBA 1.0 mg/kg/day i.p. x 4 days	10, >14, >14 >14, >14,	>13.2 \pm 1.78	0.0001

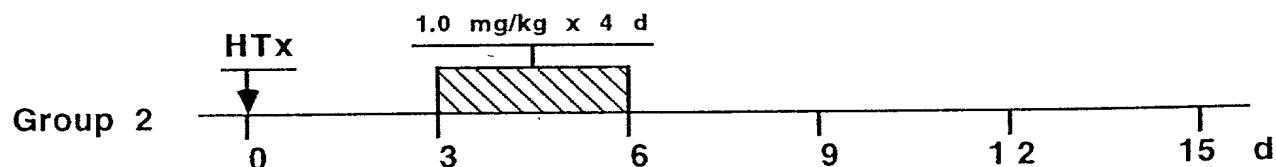


FIGURE 30

Islet Transplantation in the Mouse Model

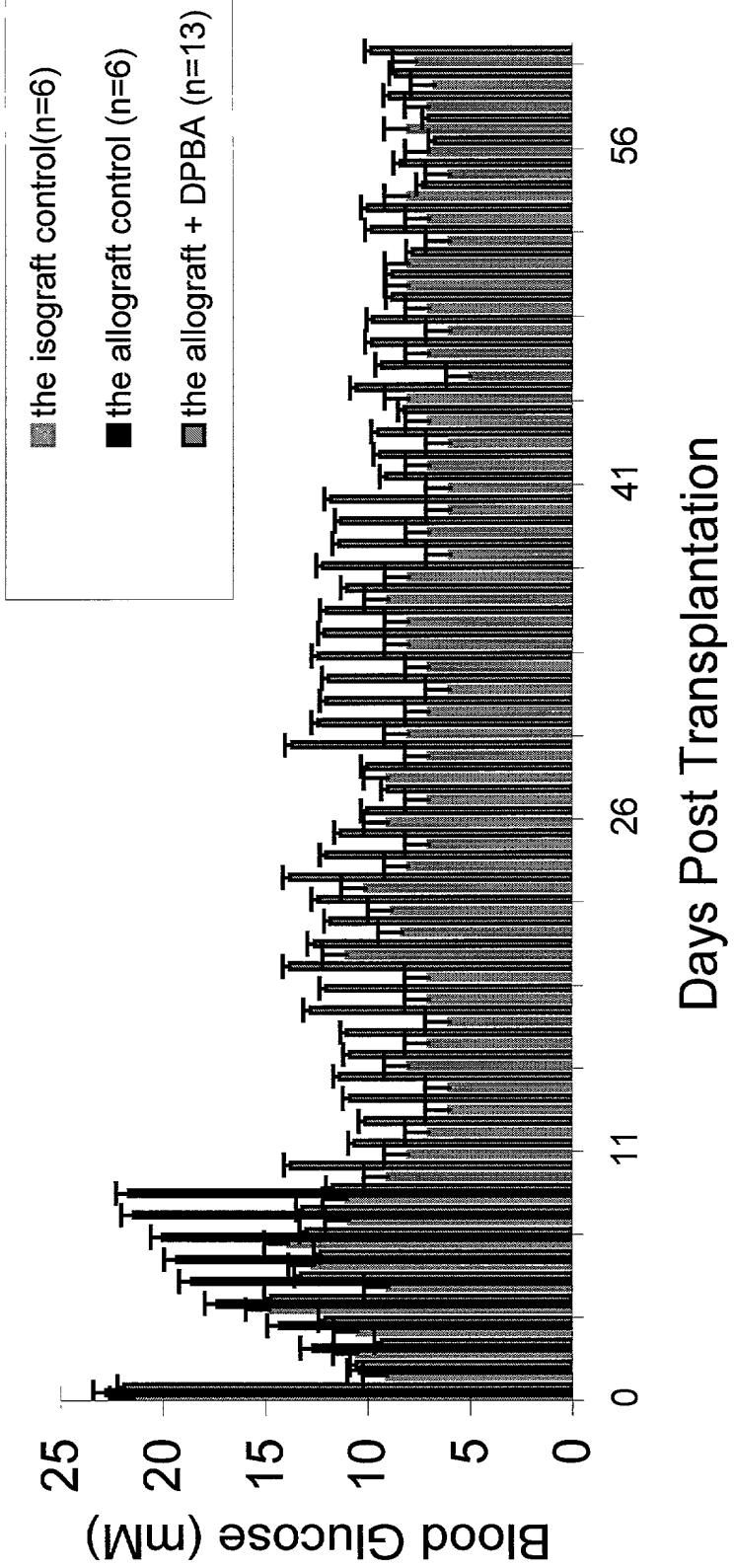


Figure 31